

CLAIMS

WHAT IS CLAIMED IS:

- 5 1. A method of enhancing the immune response of a patient relative to the normal immune response, comprising the steps of:
- growing cells containing a tumor antigen, a bacterial protein, or a viral protein under conditions wherein an aspartic acid residue or an asparagine residue in said tumor antigen, said bacterial protein, or said viral protein is converted to an isoaspartic acid residue to produce an
- 10 isoaspartic acid-containing tumor antigen, an isoaspartic acid-containing bacterial protein, or an isoaspartic acid-containing viral protein;
- optionally isolating said isoaspartic acid-containing tumor antigen, an isoaspartic acid-containing bacterial protein, or an isoaspartic acid-containing viral protein; and
- administering said cells or said isolated isoaspartic acid-containing tumor antigen, an
- 15 isoaspartic acid-containing bacterial protein, or an isoaspartic acid-containing viral protein to said patient to enhance the immune response of said patient.
2. The method of claim 1, wherein said growing step comprises exposing said cells containing said tumor antigen, said bacterial protein, or said viral protein to adenosine
- 20 dialdehyde.
3. The method of claim 1, wherein said conditions comprise exposing said cells to 15-30 μ M adenosine dialdehyde at approximately 25-40°C for 1-5 days.
- 25 4. The method of claim 1, wherein said cells are tumor cells selected from the group consisting of murine B16 melanoma, P815 murine mastocytoma, PTAS murine mammary carcinoma, colon rectal carcinoma, adenocarcinoma, glioblastoma multiform and astrosarcoma, cervical carcinoma, lung carcinomas, lymphomas, fibrosarcoma, and myeloma.
- 30 5. The method of claim 1, wherein said tumor antigen is selected from the group consisting of MART-1 (Melan-A), gp100 (pmel-17), tyrosinase, tyrosinase related protein-1 (TRP-1),

tyrosinase related protein-2 (TRP-2), melanocyte-stimulating hormone receptor, beta-catenin, MUM-1, CDK-4, Caspase-8, KIA0205, MAGE-1, MAGE-2, MAGE-3, MAGE-12, BAGE, GAGE, Ny-ESO-1, alpha-Fetoprotein, telomerase catalytic protein, G-250, MUC-1, carcinoembryonic antigen (CEA), p53, and Her-2/neu.

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6. The method of claim 1, wherein said cells are bacterial cells selected from the group consisting of Bacillus, Mycobacterium, Streptococcus, Staphylococcus, Neisseria, Chlamydia, Haemophilus, and Borrelia burgdorferi

10 7. The method of claim 1, wherein said bacterial protein is selected from the group consisting of PhoE, OmpF, OmpC; LamB, O-antigens; lipoproteins; flagella proteins; and bacterial adhesins.

8. The method of claim 1, wherein said cells are viruses selected from the group consisting of
15 Hepatitis A, Hepatitis B, Hepatitis C, Rabies, HIV, Influenza, Measles, Rotavirus, and Herpes simplex.

9. The method of claim 1, wherein said viral protein is selected from the group consisting of HIV gp120, gp41, Hepatitis B surface antigens (HBsAg), core antigen (HbcAg), and capsid proteins.

20 10. The method of claim 1, wherein said aspartic acid residue or asparagine residue comprises an amino acid sequence selected from the group consisting of Asn-Gly, Asn-Ser, Asp-Gly, and Asp-Ser.

11. A method of enhancing the immune response of a patient relative to the normal immune
25 response, comprising the steps of:

administering to said patient a peptide comprising 9-40 amino acid residues of a tumor antigen, a bacterial protein, or a viral protein, wherein said peptide comprises an aspartic acid residue or an asparagine residue that has been replaced with an isoaspartic acid residue, to enhance the immune response of said patient.

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12. The method of claim 11, wherein said peptide comprises 9-25 amino acid residues.

13. The method of claim 11, wherein said peptide comprises 9-15 amino acid residues.

14. The method of claim 11, wherein said tumor antigen is selected from the group consisting
5 of MART-1 (Melan-A), gp100 (pmel-17), tyrosinase, tyrosinase related protein-1 (TRP-1),
tyrosinase related protein-2 (TRP-2), melanocyte-stimulating hormone receptor, beta-catenin,
MUM-1, CDK-4, Caspase-8, KIA0205, MAGE-1, MAGE-2, MAGE-3, MAGE-12, BAGE,
GAGE, Ny-ESO-1, alpha-Fetoprotein, telomerase catalytic protein, G-250, MUC-1,
carcinoembryonic antigen (CEA), p53, and Her-2/neu.

15. The method of claim 11, wherein said bacterial protein is selected from the group
consisting of PhoE, OmpF, OmpC; LamB, O-antigens; lipoproteins; flagella proteins; and
bacterial adhesins.

16. The method of claim 11, wherein said viral protein is selected from the group consisting HIV
15 gp120, gp41, Hepatitis B surface antigens (HBsAg), core antigen (HbcAg), and capsid proteins.

17. The method of claim 11, wherein said aspartic acid residue or asparagine residue
comprises an amino acid sequence selected from the group consisting of Asn-Gly, Asn-Ser, Asp-
20 Gly, and Asp-Ser.

18. The method of claim 11, wherein said peptide has the sequence Tyr-Met-Asp-Gly-Thr-
Met-Ser-Gln-Val (SEQ ID NO:1).

19. A method of enhancing the immune response of a patient relative to the normal immune
25 response, comprising the steps of:

providing a tumor antigen, a bacterial protein, or a viral protein, or a fragment thereof,
wherein each of said tumor antigen, bacterial protein, or viral protein, or fragment thereof,
comprises an aspartic acid residue or an asparagine residue;

30 treating said tumor antigen, bacterial protein, or viral protein, or fragment thereof, to
convert said aspartic acid residue or said asparagine residue to an isoaspartic acid residue to

produce an isoaspartic acid-containing tumor antigen, an isoaspartic acid-containing bacterial protein, or an isoaspartic acid-containing viral protein, or fragments thereof; and

administering said isoaspartic acid-containing tumor antigen, said isoaspartic acid-containing bacterial protein, or said isoaspartic acid-containing viral protein, or fragments thereof, to said patient to elicit said enhanced immune response.

20. The method of claim 19, wherein said treating step comprises exposing said tumor antigen, said bacterial protein, or said viral protein, or said fragment thereof, to acidic methanol.

21. The method of claim 19, wherein said treating step comprises exposing said tumor antigen, said bacterial protein, or said viral protein, or said fragment thereof, to from 1-20% carbon dioxide.

22. The method of claim 19, wherein said tumor antigen is selected from the group consisting of MART-1 (Melan-A), gp100 (pmel-17), tyrosinase, tyrosinase related protein-1 (TRP-1), tyrosinase related protein-2 (TRP-2), melanocyte-stimulating hormone receptor, beta-catenin, MUM-1, CDK-4, Caspase-8, KIA0205, MAGE-1, MAGE-2, MAGE-3, MAGE-12, BAGE, GAGE, Ny-ESO-1, alpha-Fetoprotein, telomerase catalytic protein, G-250, MUC-1, carcinoembryonic antigen (CEA), p53, and Her-2/neu.

23. The method of claim 19, wherein said bacterial protein is selected from the group consisting of PhoE, OmpF, OmpC; LamB, O-antigens; lipoproteins; flagella proteins; and bacterial adhesins.

24. The method of claim 19, wherein said viral protein is selected from the group consisting of HIV gp120, gp41, Hepatitis B surface antigens (HBsAg), core antigen (HbcAg), and capsid proteins.

25. The method of claim 19, wherein said aspartic acid residue or asparagine residue comprises an amino acid sequence selected from the group consisting of Asn-Gly, Asn-Ser, Asp-Gly, and Asp-Ser.

26. A vaccine, comprising:

a protein or fragment thereof, said protein selected from the group consisting of tumor antigens, bacterial proteins, viral proteins, and combinations thereof, said protein or fragment thereof comprising an isoaspartic acid residue; and
a pharmaceutically acceptable carrier.

27. The vaccine of claim 26, wherein said pharmaceutically acceptable carrier is selected from the group consisting of solid carrier material, electrolyte solutions, anal suppositories, topical creams, sublingual lozenges, water soluble jellies, enema solutions, inhalable aerosols, intravenous injections, and combinations thereof.

28. The vaccine of claim 26, wherein said pharmaceutically acceptable carrier is selected from the group consisting of magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, low melting waxes, cocoa butter, water, and combinations thereof.

29. An antibody reactive with a protein or fragment thereof, said protein or fragment thereof comprising an isoaspartic acid residue, said protein or fragment thereof selected from the group consisting of tumor antigens, bacterial proteins, viral proteins, and combinations thereof.